REMARKS

The fee for a three-month extension of time and any other fees that may be due in connection with the filing of this paper or with this application should be charged to Deposit Account No. 02-1818. If a Petition for Extension of Time is needed, this paper is to be considered such Petition.

Claims 1 and 3-40 are pending. Claim 2 is cancelled without prejudice or disclaimer. Claim 3 is amended to depend from claim 1 and reads on the elected species. Claims 4, 6-9, 12, 21-23, 25, 32, 34 and 36, directed to non-elected species, are withdrawn. Claims 1, 7, 10, 12, 21, 24 and 25 are amended to more distinctly claim the subject matter and to correct formatting for clarity. No new matter is added.

TRAVERSAL OF SECOND FINDING OF LACK OF UNITY

The Office Action, mailed August 27, 2008, withdraws the previous restriction requirement. The Examiner acknowledges that the compound described in Dow *et al.* (WO 97/49735) does not anticipate the instantly claimed subject matter and therefore does not destroy unity.

The Examiner has cited new art and maintains that the requirement for restriction is proper. Thus, the Office Action restricts the pending claims into three groups as follows:

Group 1: claims 1-25 and 31-36, drawn to a cationic oligomer of a saccharide and methods of making the oligomers;

Group 2: claims 26, 27, 37 and 38, drawn to a method of enantiomeric separation of racemates using the cationic oligomers; and

Group 3: claims 28-30, 39 and 40, drawn to a method of asymmetric synthesis using the cationic oligomers.

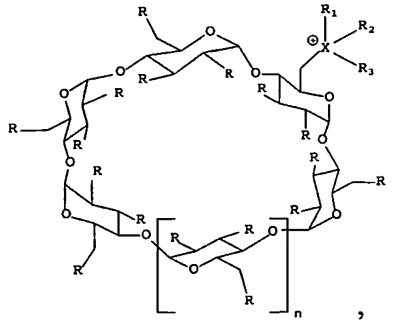
This conclusion is based upon the premise that a special technical feature shared among the groups, the cationic oligomer having only one substituent X as claimed, is disclosed in Breslow *et al.* (J Am Chem Soc 100(10: 3227-3229 (1978)). The Examiner alleges that Breslow *et al.* discloses preparing the compound β -cyclodextrinyl-6-monoimidazole by reacting a known β-cyclodextrinyl-6-monotosylate with imidazole, which the Examiner alleges results in β-cyclodextrinyl-6-monoimidazolium, which is within the scope of the instant product claims. Because β-cyclodextrinyl-6-monoimidazolium allegedly inherently is disclosed in Breslow *et al.*, the Examiner concludes that such a product cannot serve as a special technical feature unifying the claims.

Reconsideration of the Requirement respectfully is requested in view of the amendment and the following remarks.

The Claims

Independent claim 1 of Group I is directed to:

A <u>cationic</u> oligomer of a saccharide of formula (I):



, ***(I)***

wherein:

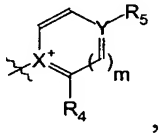
n = 0 to 8;

X is nitrogen or phosphorus;

R is a hydroxyl, an ester, a carbamate, a carbonate, a phosphinate, a phosphonate, a phosphate, a sulfinate, a sulfite, a sulfonate, a sulphate, or R'O-, wherein R' is linear or branched (C_1-C_{20})alkyl, hydroxy(C_1-C_{20})alkyl, carboxy(C_1-C_{20})alkyl, aryl, or aryl(C_1-C_{20})alkyl; and

R_1, R_2 and R_3 are each independently selected from the group consisting of hydrogen, linear or branched (C_1-C_{20})alkyl, linear or branched (C_1-C_{20})-alkenyl, linear or branched (C_1-C_{20})alkynyl, and cycloalkyl; or

R_1 is absent, and R_2 and R_3 are taken together with X to form a ring having the following structure:



,

wherein:

m = 0 or 1;

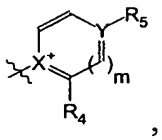
Y is carbon or nitrogen;

R_4 is hydrogen, linear or branched (C_1-C_{20})alkyl, linear or branched (C_1-C_{20})-alkenyl, linear or branched (C_1-C_{20})alkynyl, or cycloalkyl; and

R_5 is 2-(2-ethoxyethoxy)ethyl, linear or branched (C_1-C_{20})-alkyl, linear or branched (C_1-C_{20})alkenyl, linear or branched (C_1-C_{20})alkynyl, cycloalkyl, or NR_6R_7, wherein R_6 and R_7 are each independently selected from the group consisting of hydrogen, linear or branched (C_1-C_{20})alkyl, linear or branched (C_1-C_{20})alkenyl, linear or branched (C_1-C_{20})alkynyl, and cycloalkyl.

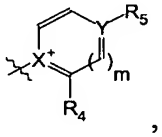
Independent claim 7 of Group I is directed to a sub-genus of the compounds of claim 1, where R_1, R_2 and R_3 are each independently selected from among hydrogen, linear or branched (C_1-C_{20})alkyl, linear or branched (C_1-C_{20})alkenyl, linear or branched (C_1-C_{20})-alkynyl, and cycloalkyl.

Independent claim 10 of Group I is directed to a sub-genus of compounds of claim 1, where R_1 is absent, and R_2 and R_3 are taken together with X to form a ring of the structure:



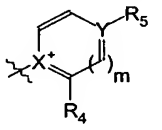
where m = 0, X is nitrogen and Y is nitrogen.

Independent claim 12 of Group I is directed to a sub-genus of the compounds of claim 1 where R_1 is absent, and R_2 and R_3 are taken together with X to form a ring having the following structure:



where m is 1, X is nitrogen, Y is carbon and R_4 is hydrogen.

Thus, a cationic oligomer of formula I is shared among the product claims of Group I. In embodiments where R_1 is absent, and R_2 and R_3 are taken together with X to form a ring having the following structure:



the heterocyclic ring includes at least one non-hydrogen substituent.

The claims of Group II are directed to methods for enantiomeric separation of a mixture of racemates using a cationic oligomer of claims of Group I as a chiral agent.

The claims of Group III are directed to methods for asymmetric synthesis of a compound using a cationic oligomer of claims of Group I as a chiral agent.

Hence, the cationic oligomer of a saccharide of claim 1 is a technical feature shared among all claims. As discussed below, the cationic oligomer of a saccharide of claim 1 is novel over the cited art. Therefore, all pending claims are unified.

Disclosure of the Cited Art and Differences from the Claimed Subject Matter

Breslow *et al.* discloses the hydrolysis of cyclic phosphate using functionalized cyclodextrin compounds as a catalyst. Breslow *et al.* discloses β-cyclodextrinyl-bis-imidazole as a model for ribonuclease catalysis. Breslow *et al.* recites a mono-functionalized cyclodextrin, β-cyclodextrinyl-6-monoimidazole, which Breslow *et al.* states is prepared from a known monotosylate (page 3228, right col., lines 2-4).

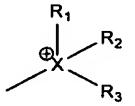
The only mono-substituted cyclodextrin disclosed in Breslow *et al.* includes a heterocyclic ring that is not substituted. Breslow *et al.* does not disclose any cyclodextrin that includes a single substitute that contains a heterocyclic ring substituted with at least one non-

hydrogen moiety. Breslow *et al.* does not describe any cyclodextrin substituted at a single position with a moiety that includes a heterocyclic ring substituted with a group selected from among 2-(2-ethoxyethoxy)ethyl, linear or branched (C_1-C_{20})-alkyl, linear or branched (C_1-C_{20})alkenyl, linear or branched (C_1-C_{20})alkynyl, cycloalkyl, or NR_6R_7, where R_6 and R_7 each independently is selected from among hydrogen, linear or branched (C_1-C_{20})alkyl, linear or branched (C_1-C_{20})alkenyl, linear or branched (C_1-C_{20})alkynyl, and cycloalkyl.

Analysis

Under PCT Rule 13 and 37 CFR §1.475(b)(3), a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn to, *e.g.*, a product, a method of making the product and a use of the product. As currently set forth, the Examiner has excluded methods of use of the products of Group I into Groups II and III. The Examiner urges that the restriction is proper because Breslow *et al.* allegedly inherently describes a species within the instantly claimed genus. The Examiner alleges that Breslow *et al.* describes preparing β-cyclodextrinyl-6-monoimidazole from β-cyclodextrinyl-6-monotosylate, which the Examiner contends results in the intermediate β-cyclodextrinyl-6-mono-imidazolium with a tosylate counterion, which is within the scope of the product claims and thus destroys unity of invention.

The functionalized β-cyclodextrin recited in Breslow *et al.* has a monoimidazole group, which is a ***charge neutral*** species. The monoimidazole substituent of Breslow *et al.* includes no non-hydrogen substituents. Hence, the β-cyclodextrinyl-6-monoimidazole mentioned in Breslow *et al.* is not within the scope of the instant claims. Breslow *et al.* does not disclose any β-cyclodextrin compounds that include a single cationic substituent of the structure



where R_1, R_2 and R_3 each independently is selected from among hydrogen, linear or branched (C_1-C_{20})alkyl, linear or branched (C_1-C_{20})-alkenyl, linear or branched (C_1-C_{20})alkynyl, and cycloalkyl, or where R_1 is absent, and R_2 and R_3 are taken together with X to form a heterocyclic ring that includes a non-hydrogen substituent. Breslow *et al.* does not describe any cyclodextrin substituted by a moiety that includes a heterocyclic ring substituted with a group selected from among 2-(2-ethoxyethoxy)ethyl, linear or branched (C_1-C_{20})-alkyl, linear or branched (C_1-C_{20})alkenyl, linear or branched (C_1-C_{20})alkynyl, cycloalkyl, or NR_6R_7, where R_6 and R_7 each independently is selected from among hydrogen, linear or branched (C_1-C_{20})alkyl, linear or branched (C_1-C_{20})alkenyl, linear or branched (C_1-C_{20})alkynyl, and cycloalkyl.

Accordingly, the charge neutral β-cyclodextrinyl-6-monoimidazole of Breslow *et al.* is not within the scope of the instant claims. Breslow *et al.* does not describe any compounds within the scope of the instant claims. Hence, the cationic derivatized cyclodextrins of the product claims of Group I are novel over the disclosure of Breslow *et al.* The claims of Group II and Group III are directed to methods of use of the compounds of claims of Group I. Thus, the instantly claimed cationic derivatized cyclodextrins of Group I are a novel technical feature shared among all claims and, at least, claims of Groups II and III are unified with the claims of Group I. Because the method of use claims of Group II are the first methods of use of the compounds restricted to Group I mentioned in the claims, at least claims of Groups I and II should be examined in this application (see 37 CFR § 1.476(c)).

REJECTION OF CLAIMS 1, 5, 10, 11, 13-20, 24, 31, 33 AND 35 UNDER 35 U.S.C. § 102(b) – Breslow *et al.*

Claims 1, 5, 10, 11, 13-20, 24, 31, 33 and 35 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Breslow *et al.* (J Am Chem Soc 100(10): 3227-3229 (1978)) because reference allegedly describes preparation of the compound β-cyclodextrinyl-6-monoimidazole by reacting imidazole with β-cyclodextrinyl-6-monotosylate, which the Examiner alleges inherently discloses the cationic β-cyclodextrinyl-6-monoimidazolium with a tosylate counter ion, which allegedly anticipates the claimed subject matter.

The rejection respectfully is traversed.

RELEVANT LAW

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. *In re Spada*, 15 USPQ2d 1655 (Fed. Cir, 1990), *In re Bond*, 15 USPQ 1566 (Fed. Cir. 1990), *Soundscriber Corp. v. U.S.*, 360 F.2d 954, 148 USPQ 298, 301, adopted 149 USPQ 640 (Ct. Cl.) 1966. See, also, *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913,1920 (Fed. Cir.), cert. denied, 110 S.Ct. 154 (1989). "[A]ll limitations in the claims must be found in the reference, since the claims measure the invention." *In re Lang*, 644 F.2d 856, 862, 209 USPQ 288, 293 (CCPA 1981). It is incumbent on Examiner to identify wherein each and every facet of the claimed invention is disclosed in the reference. *Lindemann Maschinen-fabrik Gmbh v. American Hoist and Derrick Co.*, 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984). Further, the reference must describe the invention as claimed sufficiently to have placed a person of ordinary skill in the art in possession of the invention. *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981).

THE CLAIMS

The claims are discussed above.

Disclosure of Breslow *et al.* and differences from the claimed subject matter

See related section above. The functionalized β-cyclodextrin recited in Breslow *et al.* has a monoimidazole group, which is a ***charge neutral*** species, and includes no non-hydrogen substituents. Breslow *et al.* does not describe any cyclodextrin substituted by a moiety that includes a heterocyclic ring substituted with a group selected from among 2-(2-ethoxyethoxy)-ethyl, linear or branched (C_1-C_{20})-alkyl, linear or branched (C_1-C_{20})alkenyl, linear or branched (C_1-C_{20})alkynyl, cycloalkyl, or NR_6R_7, where R_6 and R_7 each independently is selected from among hydrogen, linear or branched (C_1-C_{20})alkyl, linear or branched (C_1-C_{20})alkenyl, linear or branched (C_1-C_{20})alkynyl, and cycloalkyl. Thus, Breslow *et al.* does not disclose any cationic substituted cyclodextrin as instantly claimed.

Accordingly, for at least these reasons, Breslow *et al.* does not disclose every element of independent claims 1 and 10. Claims 5, 13-20 and 24 ultimately depend from claim 1 and include every limitation thereof. Claims 11, 31, 33 and 35 ultimately depend from claim 10 and include every limitation thereof. Thus, Breslow *et al.* does not disclose every element of claims 1, 5, 10, 11, 13-20, 24, 31, 33 and 35. Therefore, Breslow *et al.* does not anticipate any of claims 1, 5, 10, 11, 13-20, 24, 31, 33 and 35.

REJECTION OF CLAIMS 1, 5, 10, 11, 13-20, 24, 31, 33 AND 35 UNDER 35 U.S.C. 103(a)

Claims 1, 5, 10, 11, 13-20, 24, 31, 33 and 35 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Breslow *et al.* (JACS 100(10): 3227-3229 (1978)) in view of Breslow (PNAS 90:1208-1211 (1993)). The Examiner alleges that Breslow *et al.* teaches every element of the claims except that it does not specifically describe the compound β-cyclo-dextrinyl-6-monomethylimidazole, but Breslow allegedly cures this defect. This rejection respectfully is traversed.

Relevant Law

For *prima facie* obviousness of claimed subject matter to be established under 35 U.S.C. §103, all the claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). This principle of U.S. law regarding obviousness was **not** altered by the recent Supreme Court holding in KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727, 82 USPQ2d 1385 (2007). In KSR, the Supreme Court stated that "Section 103 forbids issuance of a patent when 'the differences between the subject matter sought to be patented and

the prior art are such the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.'" KSR Int'l Co. v. Teleflex Inc., 127 S.Ct. 1727, 1734, 82 USPQ2d 1385, 1391 (2007).

The mere fact that prior art may be modified to produce the claimed product does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992); see, also, In re Papesch, 315 F.2d 381, 137 U.S.P.Q. 43 (CCPA 1963). Further, that which is within the capabilities of one skilled in the art is not synonymous with that which is obvious. *Ex parte Gerlach*, 212 USPQ 471 (Bd. APP. 1980). In addition, if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Furthermore, the Supreme Court in KSR took the opportunity to reiterate a second long-standing principle of U.S. law: that a holding of obviousness requires the fact finder (here, the Examiner), to make explicit the analysis supporting a rejection under 35 U.S.C. 103, stating that "rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. Id. at 1740-41, 82 USPQ2d at 1396 (citing In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)).

While the KSR Court rejected a rigid application of the teaching, suggestion, or motivation ("TSM") test in an obviousness inquiry, the Court acknowledged the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" in an obviousness determination. KSR, 127 S. Ct. at 1731. The court stated in dicta that, where there is a

> "market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try **might** show that it was obvious under § 103."

In a post-KSR decision, PharmaStem Therapeutics. Inc. v. ViaCell. Inc., 491 F.3d 1342 (Fed. Cir. 2007), the Federal Circuit stated that:

> an invention would not be invalid for obviousness if the inventor would have been motivated to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices

> is likely to be successful. Likewise, an invention would not be deemed obvious if all that was suggested was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.

Furthermore, KSR has not overruled existing case law. See In re Papesch, (315 F.2d 381, 137 USPQ 43 (CCPA 1963)) and In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991). "In cases involving new compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." Takeda v. Alphapharm, 492 F.3d 1350 (Fed. Cir. 2007).

The disclosure of the applicant cannot be used to hunt through the prior art for the claimed elements and then combine them as claimed. In re Laskowski, 871 F.2d 115, 117, 10 USPQ2d 1397, 1398 (Fed. Cir. 1989). "To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher" W.L. Gore & Associates, Inc. v. Garlock Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983).

The Claims

The claims are discussed above.

The teachings of the cited art and differences from the claimed subject matter.

Breslow *et al.* (JACS 100(10): 3227-3229 (1978))

The teachings of Breslow *et al.* are discussed above. Breslow *et al.* recites the compound β-cyclodextrinyl-6-monoimidazole on page 3228. β-Cyclodextrinyl-6-monoimidazole is a charge neutral compound. Breslow *et al.* does not teach or suggest a positively charged *cationic* cyclodextrin derivative. The β-cyclodextrinyl-6-monoimidazole recited in Breslow *et al.* includes no non-hydrogen substituents. Breslow *et al.* does not describe any cyclodextrin substituted by a moiety that includes a heterocyclic ring substituted with a group selected from among 2-(2-ethoxyethoxy)-ethyl, linear or branched (C_1-C_{20})-alkyl, linear or branched (C_1-C_{20})alkenyl, linear or branched (C_1-C_{20})alkynyl, cycloalkyl, or NR_6R_7, where R_6 and R_7 each independently is selected from among hydrogen, linear or branched (C_1-C_{20})alkyl, linear or branched (C_1-C_{20})alkenyl, linear or branched (C_1-C_{20})alkynyl, and cycloalkyl.

Breslow (PNAS 90: 1208-1211 (1993), "Breslow 1993")

Breslow 1993 teaches a simple imidazole buffer model system for studying the kinetics and mechanism of RNA cleavage. Breslow 1993 teaches that the imidazole buffer system demonstrates a sequential bifunctional mechanism. Breslow 1993 teaches the cleavage of various RNA molecules catalyzed by imidazole buffers. Breslow 1993 teaches that N-methylimidazole buffer is similar to imidazole buffer as a catalyst. Breslow 1993 teaches that the catalysis by imidazole results in a different product than catalysis by imidazolium ion (see Fig. 1). There is no teaching in Breslow 1993 with respect to a methylimidazolium moiety or any cyclodextrin derivatives. There is no teaching or suggestion in Breslow 1993 to replace the imidazole moiety of the cyclodextrin derivatives of Breslow *et al.* with a methylimidazolium moiety or any substituent that includes a heterocyclic ring with a non-hydrogen substituent.

ANALYSIS

The combination of the teachings of Breslow *et al.* with Breslow 1993 does not result in the compositions of any of the pending claims.

Breslow *et al.* mentions the compound β-cyclodextrinyl-6-monoimidazole. The imidazole group on the cyclodextrin of Breslow *et al.* is a ***charge neutral*** species and includes no non-hydrogen substituents. There is no teaching or suggestion in Breslow *et al.* of a cationic cyclodextrin derivative as instantly claimed. There is no teaching or suggestion in Breslow *et al.* to replace the charge neutral imidazole moiety on its mono-functionalized cyclodextrin with the cationic moiety that includes a heterocyclic ring containing a non-hydrogen substituent selected from among 2-(2-ethoxyethoxy)-ethyl, linear or branched (C_1-C_{20})-alkyl, linear or branched (C_1-C_{20})alkenyl, linear or branched (C_1-C_{20})alkynyl, cycloalkyl, or NR_6R_7, where R_6 and R_7 each independently is selected from among hydrogen, linear or branched (C_1-C_{20})alkyl, linear or branched (C_1-C_{20})alkenyl, linear or branched (C_1-C_{20})alkynyl, and cycloalkyl. There is no teaching or suggestion of a methylimidazolium moiety in Breslow *et al.*

Breslow 1993 does not teach or suggest the subject matter missing from the teachings of Breslow *et al.* Breslow 1993 teaches a simple imidazole buffer model system for studying the kinetics and mechanism of RNA cleavage. There is no teaching or suggestion of a cationic substituted cyclodextrin as instantly claimed. There is no teaching or suggestion in Breslow 1993 that the reactivity of imidazole buffer is the same as an imidazole moiety covalently attached to another molecule, such as a glucose monomer of a cyclodextrin.

Breslow 1993 does not mention a methylimidazolium moiety. Breslow 1993 only teaches that *N*-methylimidazole is similar to imidazole as a catalyst. The instant claims do not encompass the charge neutral moiety *N*-methylimidazole. The instant claims recite cationic moieties that include a heterocyclic ring substituted with a non-hydrogen substituent, such as 6-deoxy-6-(methylimidazolium)-β-cyclodextrin. There is no teaching or suggestion in Breslow 1993 that a methylimidazolium substituent on a molecule, such as a cyclodextrin, has any similarity to an imidazole or an imidazolium group of a buffer system.

Neither Breslow *et al.* nor Breslow 1993, alone or in combination, teaches or suggests a 6-deoxy-6-(methylimidazolium)-β-cyclodextrin or any of the instantly claimed cationic cyclodextrin oligomers having only one cationic substituent X as instantly claimed. Therefore, for at least these reasons, the combination of Breslow *et al.* and Breslow 1993 does not teach or suggest every element of independent claims 1 or 10. Claims 5, 13-20 and 24 ultimately depend from claim 1 and include every limitation thereof. Claims 11, 31, 33 and 35 ultimately depend from claim 10 and include every limitation thereof. Therefore, the Examiner has failed to set forth a *prima facie* case of obviousness of any of the pending claims, including claims 1, 5, 10, 11, 13-20, 24, 31, 33 and 35.

* * *

In view of the amendments and remarks herein, rejoinder of Groups I and II and reconsideration and allowance of the application respectfully are requested.

Respectfully submitted,

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